

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

Claim 1 (currently amended): A method for genotyping the  $\beta_2$ AR gene of an individual, which comprises determining the identity of the nucleotide pair at the 5' leader cistron (5'LC) polymorphic site (PS) in the two copies of the  $\beta_2$ AR gene present in the individual, wherein the nucleotide pair is selected from the group consisting of: (a) cytosine and cytosine; (b) cytosine and thymine; and (c) thymine and thymine.

Claim 2 (original): The method of claim 1, wherein the determining step comprises

- (a) isolating from the individual a nucleic acid mixture comprising both copies of the  $\beta_2$ AR gene, or a fragment thereof, present in an individual;
- (b) amplifying a target region containing the 5'LC PS; and
- (c) detecting the presence of one or both of cytosine or thymine at the 5'LC PS.

Claim 3 (original): The method of claim 2, wherein the detecting step comprises:

- (a) incubating the amplified target region with MspAII; and
- (b) analyzing the incubation mixture for the presence of MspAII digestion products.

Claim 4 (original): The method of claim 2, wherein the detecting step comprises hybridizing the amplified target region with an allele-specific oligonucleotide (ASO) probe which specifically hybridizes to a  $\beta_2$ AR 5'LC allele comprising the thymine polymorphism or to a  $\beta_2$ AR 5'LC allele comprising the cytosine polymorphism.

Claim 5 (original): The method of claim 4, wherein the ASO probe comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:5, the complement of SEQ ID NO:5, SEQ ID NO:6, and the complement of SEQ ID NO:6.

Claim 6 (original): The method of claim 2, wherein the detecting step comprises sequencing the amplified target region.

*PATENT*  
*Docket No. MWH-0029US*  
*Response (to Office Actions of January 7, 2003, June 26, 2003, October 7, 2003, and December 15, 2003) filed April 14, 2004*  
*U.S. Appl. No. 09/856,803*

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**Claim 7 (original):** The method of claim 2, wherein the amplifying step is performed by the polymerase chain reaction method using at least one allele-specific primer which specifically hybridizes to a  $\beta_2$ AR 5'LC allele selected from the group consisting of a first  $\beta_2$ AR 5'LC allele comprising the thymine polymorphism, the complement of the first  $\beta_2$ AR 5'LC allele, a second  $\beta_2$ AR 5'LC allele comprising the cytosine polymorphism, and the complement of the second  $\beta_2$ AR 5'LC allele.

**Claim 8 (original):** The method of claim 7, wherein the allele-specific primer is selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:10.

**Claim 9 (withdrawn):** A method for detecting which  $[[5']]$   $\beta_2$ AR 5'LC peptide variant is expressed in an individual, which comprises contacting a biological sample from the individual with a first antibody that is specifically immunoreactive with a first 5'LC peptide variant and detecting a complex formed between the first antibody and the first 5'LC peptide variant.

**Claim 10 (withdrawn):** The method of claim 9, further comprising contacting the biological sample with a second antibody that is specifically immunoreactive with the second 5'LC peptide variant and detecting a complex formed between the second antibody and the second 5'LC peptide variant.

**Claim 11 (original):** The method of claim 1, which further comprises determining the identity of the nucleotide pair at one or more additional polymorphic sites in the  $\beta_2$ AR gene.

**Claim 12 (withdrawn):** The method of claim 10, wherein the additional polymorphic sites are selected from the group consisting of -20PS, +46PS, +79PS, +100PS and +491PS.

**Claim 13 (currently amended):** A composition comprising at least one allele-specific oligonucleotide (ASO) that specifically hybridizes to a  $\beta_2$ AR polynucleotide at a region containing the 5'LC polymorphic site, wherein the ASO is not less than 10 nucleotides in length and not more than 100 nucleotides in length.

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Claim 14 (original): The composition of claim 13, wherein the ASO is a probe comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:5, the complement of SEQ ID NO:5, SEQ ID NO:6, and the complement of SEQ ID NO:6.

Claim 15 (original): The composition of claim 13, wherein the ASO is a primer comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9 and SEQ ID NO:10.

Claim 16 (withdrawn): A method for haplotyping the  $\beta_2$ -adrenergic receptor ( $\beta_2$ AR) gene in an individual, comprising

- (a) isolating from the individual a nucleic acid molecule containing only one of the two copies of the  $\beta_2$ AR gene, or a fragment thereof, that is present in the individual; and
- (b) determining in that copy the identity of the nucleotide at the 5'LC PS and at one or more additional polymorphic sites.

Claim 17 (withdrawn): The method of claim 16, wherein the additional polymorphic sites are selected from the group consisting of -20PS, +46PS, +79PS, +100PS and +491PS.

Claim 18 (withdrawn): A method for predicting an individual's genotype for at least one coding block polymorphic site (cb PS) in the  $\beta_2$ -adrenergic receptor gene, which comprises determining the individual's genotype for the 5' leader cistron polymorphic site (5'LC PS) and assigning a genotype for the cb PS which is consistent with the individual's 5'LC PS genotype, wherein the cb PS is selected from the group consisting of +46PS and +79PS.

Claim 19 (withdrawn): A method for determining the frequency of a  $\beta_2$ AR genotype or a  $\beta_2$ AR haplotype in a population, comprising

- (a) determining the  $\beta_2$ AR genotype or the  $\beta_2$ AR haplotype pair for each member of the population and
- (b) calculating the frequency any particular  $\beta_2$ AR genotype or  $\beta_2$ AR haplotype is found in the population.

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Claim 20 (withdrawn): The method of claim 19, wherein the population is a trait population and the trait is selected from the group consisting of congestive heart failure, ischemic heart disease arrhythmia, hypertension, migraine asthma, chronic obstructive pulmonary disease (COPD), anaphylaxis, obesity, diabetes and premature labor.

Claim 21 (withdrawn): A method for identifying an association between a polymorphism in the  $\beta_2$ AR 5' leader cistron and a trait, which comprises comparing the frequency of the polymorphism in a population exhibiting the trait with the frequency of the polymorphism in a reference population, wherein a higher frequency of the polymorphism in the trait population than in the reference population indicates the polymorphism is associated with the trait.

Claim 22 (canceled)

Claim 23 (withdrawn): The method of claim 21[[22]], wherein the trait is response to an agonist or antagonist of  $\beta_2$ AR.

Claim 24 (canceled)

Claim 25 (canceled)

Claim 26 (withdrawn): A method for predicting a patient's bronchodilating response to an agonist of  $\beta_2$ AR, which comprises determining the patient's genotype for the  $\beta_2$ AR 5'LC polymorphic site, wherein a patient who is homozygous T at this site is unlikely to exhibit a bronchodilating response to the agonist and a patient who contains a C at this site is likely to exhibit a bronchodilating response against the agonist.

Claim 27 (withdrawn): The method of claim 26, wherein the agonist is albuterol.

Claim 28 (withdrawn): The method of claim 18, wherein if the genotype of the 5'LC PS is cytosine then the genotype of +46PS is guanine, and if the genotype of 5'LC PS is thymine then the genotype of +46PS is adenine.

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Claim 29 (withdrawn): The method of claim 18, wherein if the genotype of the 5'LC PS is cytosine then the genotype of +79PS is guanine, and if the genotype of 5'LC PS is thymine then the genotype of +79PS is cytosine.